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## **REMARKS**

Reconsideration of the present application in view of the above amendments and following remarks is respectfully requested. Claims 1, 6-9, and 11 were pending. As set forth above, Applicants have hereby cancelled claim 6 without prejudice to the filing of any divisional, continuation, or continuation-in-part application thereon, or directed toward the subject matter of the claims as originally filed or as subsequently amended. In addition, Applicants submit that claim 1 has been hereby amended to more clearly define the subject matter encompassed by the Applicants' invention. Support for the amendment to claim 1 is found in the application as originally filed, in part, at page 37, line 32 through page 38, line 13, and Examples 2 and 3. No new matter has been added. Therefore, claims 1, 7-9, and 11 are currently pending.

## REJECTION UNDER 35 U.S.C. §103(a)

In the Office Action dated December 28, 2004, claims 1, 8, 9 and 11 were rejected under 35 U.S.C. §103(a) as unpatentable over U.S. Patent No. 5,770,429 (Lonberg *et al.*) in view of Tomizuka *et al.* (*Nat. Genetics 16*:133, 1997 and *Proc. Nat'l Acad. Sci USA 97*:722, 2000).

Applicants respectfully traverse this ground of rejection and submit that Lonberg *et al.* and Tomizuka *et al.*, taken alone or in combination, fail to teach or suggest the claimed invention. In addition to the remarks previously made of record, Applicants respectfully submit that the mere fact that the teachings of the prior art *can* be combined or modified does not make the resultant combination *prima facie* obvious, as the prior art must also suggest the desirability of the combination (*see*, *e.g.*, *In re Fritch*, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992)). A *prima facie* case of obviousness has not been established because no evidence has been provided that, at the time of filing the instant application, a person having ordinary skill in the art would have been motivated to arrive at the claimed invention.

Nevertheless, however, without acquiescing to the instant rejection, Applicants submit that the instant rejection has been rendered moot in view of the amendment to claim 1. Accordingly, Applicants respectfully request that this rejection be withdrawn.

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In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

Dated: March 28, 2005

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